

IMPORTANT NOTE: The CryoBlator Cryoablation catheters are sterile. The CryoCor console is not sterile.

CAUTION:

- United States law restricts this device to sale by or on order of a physician.
- Do not attempt to use the device before completely reading and understanding the instructions for use.

Instructions for Use

CryoCor

 **CRYOBLATOR™**

**10F Cryoablation
Catheter**

Model 1205, 1207

DEVICE DESCRIPTION

The CryoCor CryoBlator 10F Cryoablation Catheter is a single use, 10F, uni-directional steerable ablation catheter. The flexible distal section can be deflected by displacement of an integral tendon controlled by a lever on the handle. A variable manual locking feature or “brake” is provided to lock or hold the deflection angle. The proximal shaft is more rigid to allow torque transmission to the distal end of the shaft. A metal end-tip provides therapy delivery. Target tissue in contact with the tip is ablated by cooling achieved via the vaporization of refrigerant fluids inside the catheter tip assembly. A temperature sensor, located within the tip, provides temperature monitoring during therapy delivery. The tip, along with an additional 1.3mm wide band electrode spaced 3 mm proximal to the tip, also

has the ability to collect intracardiac electrograms for mapping procedures. The catheter is connected to the CryoCor Cryoablation Console, Model 2020, via three quick-connect receptacles: one for refrigerant gas, a second for pressure monitoring inside the tip and a third for electrical signal transmission.

INDICATIONS

The CryoCor Cryoablation System is intended for use in the ablation of isthmus-dependent right atrial flutter in patients 18 years of age or older.

CONTRAINDICATIONS

Do not use this device:

- in patients with active systemic infection;
- in patients with intracardiac mural thrombus or in patients who have had a ventriculotomy or atriotomy within the preceding four weeks; and
- in patients with cryoglobulinemia

Potential Risks

Potential adverse events that maybe associated with catheterization and/or cardiac ablation include:

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| • Abnormal vision | • Local hematomas/ecchymosis |
| • Adult Respiratory Distress Syndrome (ARDS) | • Myocardial infarction |
| • Air embolism | • Neck/pain/groin pain |
| • Anaphylaxis | • Obstruction or perforation or damage to the vascular system |
| • Anemia | • Palpitations |
| • Allergic reaction (anesthesia) | • Pericardial effusion |
| • Arrhythmias | • Pericarditis |
| • AV fistula | |

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| <ul style="list-style-type: none"> • Bleeding • Cardiac perforation/tamponade • Cardiac thromboembolism • Catheter rupture and release of refrigerant • Cerebrovascular accident (CVA) • Chest pain/discomfort • Complete heart block • Component damage to ICD or implantable pacemaker • Congestive heart failure/exacerbation • Coronary artery spasm • Death • Dislodgement of implantable cardioverter defibrillator or permanent pacing leads • Dizziness • Endocarditis • Exacerbation of pre-existing atrial fibrillation • Expressive aphasia • Heart Failure • Hemothorax • Hypoxia/shortness of breath • Infections/sepsis • Laceration | <ul style="list-style-type: none"> • Pleural effusion • Pneumonia • Pneumothorax • Pseudoaneurysm • Pulmonary edema • Pulmonary embolism • Radiation injury • Respiratory Depression • Seizure • Syncope/near syncope • Temporary complete heart block • Thrombi • Thromboembolism • Transient ischemic attack (TIA) • Unintended (in)complete AV, sinus node or other heart block or damage • Valvular damage/insufficiency • Vascular bleeding • Vasovagal reactions • Ventricular tachycardia • Worsening chronic obstructive pulmonary disease |
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Potential Risks Unique to the Cryoablation Procedure

There is one identified potential risk unique to pulmonary vein cryoablation procedures, namely catheter rupture and release of refrigerant gas.

WARNINGS

- Catheter ablation should only be performed after adequate attention has been given to the potential radiation exposure associated with the procedure, and steps have been taken to minimize this exposure. Careful consideration must therefore be given for this use of the device in pregnant women.
- Catheter materials are not compatible with magnetic resonance imaging (MRI).
- Catheter entrapment within the heart or blood vessels is a possible complication of electrophysiology procedures.
- Do not use force to advance or withdraw catheter when resistance is encountered.
- Do not attempt to manipulate or move the catheter tip during therapy delivery or until the tip temperature has reached a level higher than 20° C.
- The CryoCor Cryoablation Console is capable of delivering significant cryoablation therapy. When operating, do not touch the catheter tip because operator injury may occur.
- The CryoCor CryoBlator Cryoablation Catheter is disposable and intended for single use. Do not re-sterilize or reuse. This may result in a loss of cryoablation, electrical and mechanical function and could cause patient injury and/or death.
- Use only isolated ECG amplifiers with the CryoCor Cryoablation System. Leakage current from a connected device to the patient must not exceed 10 microamps (µA).

- If the catheter develops a leak, patient injury or death may occur.
- Caution should be used when delivering cryotherapy as structures located beyond the target tissue may be affected.
- Careful catheter manipulation must be performed in order to avoid cardiac damage, perforation, or tamponade. Catheter advancement should be done under fluoroscopic guidance. Do not use excessive force or torque to advance, withdraw, or manipulate the catheter.
- During therapy delivery, the catheter tip will become attached to the target tissue. Do not attempt to manipulate or move the catheter tip during therapy delivery.
- Following therapy delivery, do not manipulate the catheter tip until the "Wait to Remove Catheter" message on the Console LCD has disappeared. This provides sufficient time for the catheter tip to thaw and detach itself from the target tissue.
- The CryoCor Cardiac Cryoablation System can not be used at altitudes that are greater than 3600 feet.
- The CryoCor Cryoablation System has not been studied in patients with structural heart disease of clinical significance including patients with:
 - Cardiac surgery within six months of screening
 - Unstable symptoms of congestive heart failure (CHF) including NYHA Class III or IV CHF at screening and/or ejection fraction <30% as measured by ECHO or catheterization
 - Right-sided heart valve prosthetics
 - Myocardial infarction (MI) within three months of screening
 - Unstable angina or ongoing myocardial ischemia
 - Corrected or uncorrected atrial septal defect (ASD)
 - Congenital heart disease where either the underlying abnormality or its correction prohibits or increases the risk of cryoablation
- Presently, there is no available data to support the safety and effectiveness of the use of the CryoCor Cryoablation System in the left heart.

PRECAUTIONS

- The sterile packaging and catheter should be visually inspected prior to use. Inspect for holes in the packaging and compromise to the seal prior to opening and removal of catheter. If damaged, do not use. Inspect the catheter for damage to the shaft, exposed wire(s) or tubing and damaged connectors.
- Do not attempt to operate the Cryoablation System before thoroughly reading the Operators Manual.
- The LCD on the Console should be monitored during therapy delivery.
- Excessive bending or kinking of the catheter shaft and/or flex interconnect may damage internal components. Manual pre-bending of the distal curve can damage the steering and/or deployment mechanism and may lead to patient injury.
- Cardiac ablation procedures should be performed only by physicians thoroughly trained in the techniques of catheter ablation in a fully equipped electrophysiology laboratory.
- It is important that the physician determines, assesses and communicates to each individual patient all foreseeable risks of a cardiac ablation procedure.
- The CryoCor Cryoablation Console is intended for use only with CryoCor Cryoablation Catheters and accessories. The safety of use with other electrophysiology catheters and accessories has not been assessed.
- Prior to delivery of ablation therapy, ensure catheter tip is beyond the end of the sheath.
- Do not articulate the catheter when the articulation segment is constrained within the sheath, as articulation function may be compromised.

DIRECTIONS FOR USE

Preparing the CryoCor CryoBlator 10F Cryoablation Catheter

1. Using sterile technique, remove the catheter from the package and place in a sterile work area.
2. Visually inspect the catheter carefully for integrity (cuts, punctures) and overall condition. If damaged, do not use: return to CryoCor.
3. Manipulate handle to confirm steering function.
4. Maintain the black plastic end cap on the main gas connector whenever the catheter is not connected to the Console.

Insertion and Placement of CryoCor CryoBlator 10F Cryoablation Catheter

1. Create appropriate vascular access site to introduce catheter to reach desired locations within the heart.
 - Approach through the femoral vein utilizing standard 10F or larger percutaneous hemostasis sheath.
2. Ensuring that the tip of the catheter is in its relaxed or non-articulated position, advance the catheter through the vasculature and into the heart under fluoroscopic guidance. Use the lever control on the catheter to facilitate positioning of the catheter tip.

NOTE: During manipulation, the catheter may be disconnected from the control arm of the Console in order to avoid twisting and tangling of cables and connections.

Connect Catheter To Console

NOTE: The control arm on the Console is non-sterile. Ensure that, when making or breaking connection to the control arm, care is taken to avoid contact with the Console.

1. Twist and remove the black plastic end cap from the main gas connector on the proximal end of the catheter and let it hang by the metal chain.
2. Remove black precooler plug from the precooler receptacle located on the control arm of the Console.
3. Align the gas connector with the mating receptacle on the control arm of the Console (non-sterile) and push the gas connector in until it latches. To disconnect, grasp the black sleeve on the connector and pull back until the connector disengages. Following disconnection of the gas connector, replace the plastic end cap to avoid contamination within the sterile field and replace precooler plug on control arm.

NOTE: This connection is not keyed and can rotate freely.

4. Locate the Luer at the proximal end of the catheter and align it with the mating receptacle at the end of the console arm. Grasp the body of the Luer and twist until a snug connection has been made. To disconnect, grasp the body of the Luer and twist the Luer fitting counter clockwise until the Luer is disconnected.
5. Locate the electrical connector and attach it to the receptacle located on the distal end of the control arm of the Console by aligning the key on the connector with the key indicator on the receptacle while pushing together until connector has latched.

NOTE: If the physician chooses to disconnect the sensor cable from the console once it has been connected, care must be taken not to contaminate the sterile field by the now contaminated end of the sensor cable. Disconnection of the sensor cable at the catheter end prevents contamination. For removal of the sensor cable, grasp the gray sleeve on the connector and pull back until the connector disengages from the receptacle.

THERAPY DELIVERY

1. Prior to delivery of ablation therapy, ensure that the catheter tip is in direct contact with the target tissue.
2. During therapy delivery, the catheter tip will become attached to the target tissue. Do not attempt to manipulate or move the catheter tip during therapy delivery.
3. Following therapy delivery, do not manipulate the catheter tip until the tip temperature reaches at least 20° C. This provides sufficient time for the catheter tip to thaw and detach itself from the target tissue.

POST-PROCEDURE CATHETER REMOVAL

1. Prior to removing the CryoCor CryoBlator 10F Cryoablation Catheter, ensure that the catheter is in its relaxed or non-articulated position.
2. Slowly withdraw the catheter from the patient. Should any resistance be encountered withdrawing the catheter into the sheath, the catheter and the sheath should be removed as a single unit."
3. Remove the hemostasis sheath, and follow standard practice for management of the insertion site.
4. Follow standard practice for disposal of used medical devices.

STORAGE AND HANDLING

Store in a cool, dark, dry place.

SPECIFICATIONS

Catheter Diameter..... 10F (3.3mm)


Usable Length--


Model:  CRYOBLATOR[®] -05: 95 cm

Model:  CRYOBLATOR[®] -07: 97 cm

Tip Length..... 6.5 mm

Articulation Segment Length--

Model:  CRYOBLATOR[®] -05: 5 cm

Model:  CRYOBLATOR[®] -07: 7 cm

Deflection Angle >180° (uni-directional)

Band Electrode Width..... 1.3 mm

Band Electrode Spacing (from tip) 3 mm

Summary of Clinical Studies

A. Study Design

The CryoCor™ Cardiac Cryoablation System was evaluated in a prospective, non randomized single-arm, multicenter trial conducted in 160 subjects at 24 U.S. sites to evaluate the safety and effectiveness of the system. Subjects with a recent history of symptomatic, cavo-tricuspid isthmus-dependent atrial flutter were eligible. Subjects were evaluated at discharge, one, three and (via telephone) six months post-procedure as well as weekly via trans-telephonic event recordings collection. Subjects who met the inclusion and exclusion criteria were enrolled.

1. Inclusion Criteria

Subjects were eligible for inclusion in the study if they met all of the following Inclusion Criteria:

- Age between 18 and 75
- Symptomatic atrial flutter with at least one episode within the last six months, documented on ECG
- Documentation of isthmus-dependent right-atrial flutter as evident from pacing and/or mapping (performed in the EP lab just prior to ablation)
- Willingness, ability and commitment to participate in follow-up evaluations

2. Exclusion Criteria

Subjects were excluded from the study if any of the following conditions were present:

- Structural heart disease of clinical significance including:
 - Cardiac surgery within six months of screening
 - Unstable symptoms of congestive heart failure (CHF) including NYHA Class III or IV CHF at screening and/or ejection fraction <30% as measured by ECHO or catheterization
 - Right-sided heart valve prosthetics
 - Myocardial infarction (MI) within three months of screening
 - Unstable angina or ongoing myocardial ischemia
 - Corrected or uncorrected atrial septal defect (ASD)
 - Congenital heart disease where either the underlying abnormality or its correction prohibits or increases the risk of cryoablation
- Any prior ablation for atrial flutter
- Any prior ablation (other than atrial flutter) within three months of screening
- Concomitant atrial fibrillation requiring AAD treatment other than Class IC or Class III for conversion to atrial flutter
- Any concomitant ventricular arrhythmia requiring pharmacological treatment that would interfere with the interpretation of the results from this study

- Severe electrolyte abnormalities at the time of treatment
- Pregnancy
- Any contraindication to cardiac catheterization
- Poor general health that, in the opinion of the investigator, will not allow the subject to be a good study candidate (i.e. other disease processes, mental capacity, etc.)
- Enrollment in any other ongoing protocol

3. Prior and Concomitant Therapies Allowed

Subjects with concomitant atrial fibrillation (AF) requiring drug therapy, other than with Class IC or Class III antiarrhythmic drugs, for conversion to atrial flutter were excluded from the study. The study allowed inclusion of subjects with a history of AF who had converted to symptomatic atrial flutter when placed on anti-arrhythmic drugs (specifically Class IC and Class III drugs). After cryoablation was performed, the continuation, discontinuation or modification of all pre-procedure Class IC and Class III drugs for the purpose of AF control was at the discretion of the investigator.

B. Study Objectives

1. Study Primary Endpoints

The primary endpoints were the following acute safety and effectiveness measures:

- Measurement of all serious adverse events (SAEs) that occurred within seven days after the procedure
- Creation of bi-directional block with cryoablation as the surrogate measure of procedural effectiveness

2. Study Secondary Objectives

The secondary objectives were the following chronic safety and effectiveness measures:

- Measurement of serious adverse events that occurred more than seven days after the cryoablation procedure
- Long-term absence of recurrences of atrial flutter (chronic effectiveness)
- Re-treatment effectiveness

C. Objective Performance Criteria (OPC)

Objective Performance Criteria (OPC) were prospectively established for this study. The performance goals for this study were taken from the FDA guidance document "Cardiac Ablation Catheters Generic Arrhythmia Indications for Use; Guidance for Industry, July 1, 2002." See table 1 below for the endpoints used.

Table 1 - Objective Performance Criteria

Study Endpoint	Target Value	95% Confidence Bound
Acute Success	> 95%	≥ 80%
Chronic Success	>90%	≥ 80%
7 Day SAEs	< 2.5%	≤7%

D. Patient Enrollment and Disposition

Table 2 below documents the enrollment and disposition of the patients screened for the study.

Table 2 - Patient Enrollment and Disposition

Patients screened for the study	189
Screen Failures	28
Isthmus-dependent atrial flutter not inducible	26
Persistent atrial fibrillation	1
Non-investigational device failure	1
Patient withdrew consent before treatment	1
CryoCor cryoablation investigational catheter inserted (Intent-to-Treat)	160

E. Demographic Data

Of the 160 treated patients, 122 (76.25%) were men and 155 (96.88%) were Caucasian. The mean age of patients enrolled in the study was 63.06 ± 9.25 years. One hundred and four (104) (65%) of these patients reported concomitant arrhythmias in addition to atrial flutter. Atrial fibrillation was the most common among these reported concomitant arrhythmias (58.75%). The majority of patients presented with counterclockwise atrial flutter (78.75%). Treated patients had a mean ejection fraction (EF) of $54.62 \pm 10.44\%$.

F. Procedural Data

An effective cryotherapy application was determined to be a freeze which resulted in an electrophysiological effect as seen on the EGM. The patients enrolled in the study had an average of 20 (± 11.34) freezes delivered during the ablation with an average of 18 (± 9.3) being effective. The average temperature of each freezes was $-81.52 (\pm 3.73)$ degrees Centigrade with the lowest temperature of $-85.56 (\pm 3.61)$ being reported.

Table 3 - Characteristics of Delivered Cryotherapy

Description	Mean	SD
# of Freezes	20.45	11.34
# of Effective Freezes	18.61	9.30
Freeze Duration (min:sec)	47:36	24:34
Average Temp	-81.52	3.73
Minimum Temp	-85.56	3.61

G. Primary Endpoint: Acute Safety

The 7 day SAE rate after the index procedure is listed in the table below. Out of the 10 events, only 4 were classified as related to the device or the procedure. The device-related and procedure-related SAEs occurring within 7 days included one case each of post procedural hematoma , atrioventricular block complete, cardiac tamponade and acute respiratory failure. All four of these SAEs were resolved by the end of the study.

Table 4: Acute Safety Data

Study Endpoint	Patient Count	Percent	95% One-Sided CL
Acute Safety			
7 Day SAEs	9/160	5.63%	UCL: 9.61%
7 Day SAEs (D&P)*	4/160	2.50%	UCL: 5.63%

Table 5: Acute Safety (7-day Serious Adverse Events)

Description	Events				Patients	
	Mild	Mod	Severe	Total	Total	Pct
Atrial Flutter	0	1	0	1	1	(0.63%)
Sick Sinus Syndrome	0	1	1	2	2	(1.25%)
Acute Respiratory Failure *	0	0	1	1	1	(0.63%)
Atrial Fibrillation	0	0	1	1	1	(0.63%)
Atrioventricular Block-Complete*	0	1	0	1	1	(0.63%)
Cardiac Tamponade *	0	0	1	1	1	(0.63%)
Dizziness	0	1	0	1	1	(0.63%)
Hyperthyroidism	0	0	1	1	1	(0.63%)
Post Procedural Hematoma*	0	1	0	1	1	(0.63%)

* Device and Procedure related

H. Primary Endpoint: Acute Effectiveness

The acute procedural success is listed in the table below. One subject had the catheter inserted, but no cryoablation was performed. This patient was removed from the analysis.

Table 6: Acute Procedural Success

Patient Count	Percent	95% One-Sided CL
140/159	88.05%	LCL:82.96%

I. Secondary Objective: Chronic Safety

The rate of SAEs occurring more than 7 days after the index procedure is listed in the table below. None of these were related to the device or procedure.

Table 7: Chronic Safety

Study Endpoint	Patient Count	Percent	95% One-Sided CL
Chronic Safety			
SAEs post-7 days	28/160	17.50%	UCL: 23.06%

Three (3) subjects died during the course of the study. The deaths were not related to the device or ablation procedure. The causes of death included: suicide, illicit drug overdose and pulmonary emboli.

J. Secondary Objective: Chronic Effectiveness

The chronic effectiveness was conditional on acute effectiveness and was determined by clinical follow-up with clear documentation of recurrences in addition to weekly event recordings to evaluate asymptomatic recurrences. Patients were considered a success if they were without any objective evidence (i.e., documented on event recordings, Holter, ECG, etc.) of atrial flutter for 6 months. The primary analysis for the secondary objective was a time-to-event analysis or Kaplan-Meier nonparametric survival. Subjects who did not have a complete set of data for the six-month post-procedure follow-up period were censored at their last known visit or documented event recording if they had not yet recurred.

The chronic effectiveness results are listed in the table below.

Table 8: Chronic Effectiveness

Analysis	Proportion Free From AFL Recurrence	95% CI Lower Bound
Survival Estimate	81.60%	74.70% (Peto)

A *post hoc* analysis of chronic effectiveness was conducted which considers all subjects in whom the cryoablation catheter was inserted and cryoablation energy was applied, regardless of whether the subject was an acute effectiveness success. Patients who died (all for reasons unrelated to the procedure) and those patients that were non-compliant with follow-up were excluded from this analysis. Using this definition, 106 out of 151 (70.2%) of all patients undergoing cryoablation treatment exhibited long-term freedom from cavo-tricuspid isthmus dependent atrial flutter. In a worst case scenario where all censored patients are considered failures, the long-term freedom-from-flutter rate is 66.7% (106 out of 159).

K. Secondary Objective: Retreatment Effectiveness

Five subjects were re-treated with cryoablation and five subjects were re-treated with RF ablation after recurrence of atrial flutter. One subject was first re-treated with cryoablation, and after an additional recurrence, was re-treated with radio frequency ablation. Subjects re-treated with cryoablation were asked to continue sending in weekly random and symptomatic event recordings until they completed the study. The subjects re-treated with radio frequency were optionally offered the opportunity to continue with event recording. Of the five subjects who were re-treated with cryoablation after recurrence of atrial flutter, one subjects experienced recurrence after re-treatment, and was subsequently

treated with radiofrequency ablation. Due to the small sample size, no statistical calculations were performed.

XI. Conclusions Drawn from the Studies

Pre-clinical testing adequately demonstrates that the CryoCor Cardiac Cryoablation System, developed by CryoCor, Inc., should maintain mechanical and electrical integrity and that materials which come in contact with patients should be biocompatible under the proposed conditions for use. Bench testing has established an acceptable degree of energy delivery accuracy and control.

Clinical testing and statistical analysis demonstrates that there is a reasonable assurance of safety and effectiveness for the CryoCor Cardiac Cryoablation System for the treatment of right atrial isthmus dependant flutter.



**10F Cryoablation Catheter
Model 1205, 1207**

One sterile CryoCor CryoBlator 10F Cryoablation Catheter

Non-pyrogenic

No warranty implied

Contents are for single use. Do not attempt to resterilize.

Read instructions prior to use.

Sterilization: Radiation

Caution: Federal (USA) law restricts this device to use by or on the order of a physician.

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